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|--------------------------|------------------|---------------|--|
| Interview Summary | Application No. | Applicant(s) | |
| | 09/822,161 | DETMAR ET AL. | |
| | Examiner | Art Unit | |
| | MISOOK YU, Ph.D. | 1642 | |

All participants (applicant, applicant's representative, PTO personnel):

- (1) MISOOK YU, Ph.D. (3) Michelle Iwamoto.
 (2) Thomas Kowalski. (4) _____.

Date of Interview: 09 July 2003.

Type: a) ☒ Telephonic b) ☐ Video Conference
 c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☒ Yes e) ☐ No.
 If Yes, brief description: fax and email.

Claim(s) discussed: 1-7, and 16-29.

Identification of prior art discussed: _____.

Agreement with respect to the claims f) ☐ was reached. g) ☐ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Applicant argued the provisional application 60/127,221 provide adequate support, the specification provide enablement how to use anti-angiogenic molecule, the support for angiostatin and endostatin is at page 7.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

 Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

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FACSIMILE COVER LETTER

To: Examiner: Misook Yu
Firm:
Facsimile: (703) 746-7647
From: Michelle Akiko Iwamoto, Ph.D.
Date: June 30, 2003
Re: Our Reference No.: 91000-2020
Number of Pages: 5
(including cover page)
cc:

If you do not receive all pages or are unable to read the transmission, please call and ask for Anna Mendoras (Ext. 2068).

NOTE:

This draft is to be considered for discussion purposes only.

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Document12

Draft for Discussion Purposes Only**Claims Filed in US Application No. 09/822,161:****DRAFT FOR DISCUSSION PURPOSES ONLY**

1. (Amended) A method for treating a disorder characterized by excessive proliferation of tissue comprising implanting a cell-matrix structure in an amount effective to inhibit or regress the excessive tissue proliferation, wherein said cell-matrix structure comprises a matrix having attached thereto cells stably expressing a gene encoding an anti-angiogenic molecule.
2. The method of claim 1 wherein the disorder is selected from the group consisting of malignant and benign neoplasias, vascular, inflammatory conditions causing excessive proliferation of cells, keloid formation, intraperitoneal or intrathoracic adhesions, endometriosis, congenital or endocrine abnormalities, psoriasis, unwanted skin proliferation, rheumatoid arthritis, multiple sclerosis, unwanted angiogenesis of the eye, restenosis, and infections causing excessive proliferation of cells.
3. The method of claim 1 wherein the matrix is selected from the group consisting of fibrous scaffolds, polymeric hydrogels, and micromachine or micromolded substrates.
4. The method of claim 1 wherein the cells are selected from the group consisting of fibroblasts, tissue specific cells, progenitor cells, and stem cells.
5. (Amended) The method of claim 1 wherein the cells are genetically engineered to produce the anti-angiogenic molecule.
6. (Amended) The method of claim 1 wherein the anti-angiogenic molecule is thrombomodulin.
7. The method of claim 1 wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule.

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8. A cell-matrix structure for implantation into a patient having attached thereto an effective amount of cells stably expressing a gene encoding an anti-angiogenic molecule in an effective amount to inhibit or regress excessive tissue proliferation in a patient in need thereof, wherein the cells are either genetically engineered to produce the anti-angiogenic molecule or of a different cell type than the tissue that has proliferated excessively which produces the anti-angiogenic molecule.

9. The cell-matrix structure of claim 8 wherein the cells produce a anti-angiogenic molecule effective to treat a disorder is selected from the group consisting of malignant and benign neoplasias, vascular, inflammatory conditions causing excessive proliferation of cells, keloid formation, intraperitoneal or intrathoracic adhesions, endometriosis, congenital or endocrine abnormalities, psoriasis, unwanted skin proliferation, rheumatoid arthritis, multiple sclerosis, unwanted angiogenesis of the eye, restenosis, and infections causing excessive proliferation of cells.

10. The cell-matrix structure of claim 8 wherein the matrix is selected from the group consisting of fibrous scaffolds, polymeric hydrogels, and micromachine or micromolded substrates.

11. The cell-matrix structure of claim 8 wherein the cells are selected from the group consisting of fibroblasts, tissue specific cells, progenitor cells, and stem cells.

12. The cell-matrix structure of claim 8 wherein the cells are genetically engineered to produce the anti-angiogenic molecule.

13. The cell-matrix structure of claim 8 wherein the anti-angiogenic molecule is thrombomodulin.

14. The cell-matrix structure of claim 8 wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule.

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15. The cell-matrix structure of claim 8 wherein the cells are selected based on natural production of the wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule and the cells are implanted at a site where the wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule in an amount effective to inhibit proliferation or cause tissue regression.

16. (New) A method for treating a disorder characterized by excessive proliferation of tissue comprising implanting a cell-matrix structure in an amount sufficient to stop or regress the excessive tissue proliferation, wherein said cell-matrix structure comprises a matrix having attached thereto cells stably expressing a gene encoding a thrombospondin-2 (TSP-2).

17. (New) The method of claim 16, wherein the disorder is selected from the group consisting of malignant and benign neoplasias, vascular, inflammatory conditions causing excessive proliferation of cells, keloid formation, intraperitoneal or intrathoracic adhesions, endometriosis, congenital or endocrine abnormalities, psoriasis, unwanted skin proliferation, rheumatoid arthritis, multiple sclerosis, unwanted angiogenesis of the eye, restenosis, and infections causing excessive proliferation of cells.

18. (New) The method of claim 16, wherein the matrix is selected from the group consisting of fibrous scaffolds, polymeric hydrogels, and micromachine or micromolded substrates.

19. (New) The method of claim 16, wherein the cells are selected from the group consisting of fibroblasts, tissue specific cells, progenitor cells, and stem cells.

20. (New) The method of claim 16, wherein the cells are genetically engineered to produce TSP-2.

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21. (New) The method of claim 16, wherein TSP-2 is endogenous to the cells on the matrix and the cells are engineered to increase expression of TSP-2.

22. (New) The method of claim 16 wherein the cells are of a different cell type than the tissue that has proliferated.

23. (New) The method of claim 16 wherein the cells are selected based on natural production of TSP-2.

24. (New) The method of claim 1 wherein the cells are of a different cell type than the tissue that has proliferated.

25. (New) The method of claim 1 wherein the cells are selected based on natural production of the anti-angiogenic molecule.

26. (New) The method of claim 1 wherein the anti-angiogenic molecule is thrombomodulin.

27. (New) The method of claim 1 wherein the anti-angiogenic molecule is angiostatin.

28. (New) The method of claim 1 wherein the anti-angiogenic molecule is endostatin.

29. (New) The method of claim 1 wherein the anti-angiogenic molecule is TSP-1

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FACSIMILE COVER LETTER

To: Examiner Misook Yu
Firm:
Facsimile: (703) 746-7647
From: Michelle Iwamoto, Ph.D.
Date: July 8, 2003
Re: Application No. 09/822,161 (Our Ref: 910000-2020)
Number of Pages: 5
(including cover page)
cc:

If you do not receive all pages or are unable to read the transmission, please call and ask for Michelle Iwamoto (Ext. 2628).

Note:
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910000-2020

Suggested Claims For US Application No. 09/822,161:

DRAFT FOR DISCUSSION PURPOSES ONLY

1. (Currently Amended) A method for treating a disorder characterized by excessive proliferation of tissue in a subject in need thereof comprising implanting a cell-matrix structure ~~in an amount effective to inhibit or regress the excessive tissue proliferation~~, wherein said cell-matrix structure comprises a matrix having attached thereto cells that stably expressing a gene ~~encoding~~ an anti-angiogenic molecule in an amount effective to inhibit or regress the excessive tissue proliferation.
2. (Original) The method of claim 1 wherein the disorder is selected from the group consisting of malignant and benign neoplasias, vascular, inflammatory conditions causing excessive proliferation of cells, keloid formation, intraperitoneal or intrathoracic adhesions, endometriosis, congenital or endocrine abnormalities, psoriasis, unwanted skin proliferation, rheumatoid arthritis, multiple sclerosis, unwanted angiogenesis of the eye, restenosis, and infections causing excessive proliferation of cells.
3. (Original) The method of claim 1 wherein the matrix is selected from the group consisting of fibrous scaffolds, polymeric hydrogels, and micromachine or micromolded substrates.
4. (Original) The method of claim 1 wherein the cells are selected from the group consisting of fibroblasts, tissue specific cells, progenitor cells, and stem cells.
5. (Previously Amended) The method of claim 1 wherein the cells are genetically engineered to produce the anti-angiogenic molecule.
6. (Currently Amended) The method of claim 1 wherein the anti-angiogenic molecule is ~~thrombomodulin~~ TSP-2.

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7. (Original) The method of claim 1 wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule.

8. (Currently Amended) A cell-matrix structure for implantation into a patient in need thereof having attached thereto an effective amount of cells that stably expressing a gene encoding an anti-angiogenic molecule ~~in an effective amount to inhibit or regress excessive tissue proliferation in a patient in need thereof~~, wherein the cells are either genetically engineered to produce the anti-angiogenic molecule or of a different cell type than the tissue that has proliferated excessively, which produces the anti-angiogenic molecule in an effective amount to inhibit or regress excessive tissue proliferation.

9. (Original) The cell-matrix structure of claim 8 wherein the cells produce an anti-angiogenic molecule effective to treat a disorder is selected from the group consisting of malignant and benign neoplasias, vascular, inflammatory conditions causing excessive proliferation of cells, keloid formation, intraperitoneal or intrathoracic adhesions, endometriosis, congenital or endocrine abnormalities, psoriasis, unwanted skin proliferation, rheumatoid arthritis, multiple sclerosis, unwanted angiogenesis of the eye, restenosis, and infections causing excessive proliferation of cells.

10. (Original) The cell-matrix structure of claim 8 wherein the matrix is selected from the group consisting of fibrous scaffolds, polymeric hydrogels, and micromachine or micromolded substrates.

11. (Original) The cell-matrix structure of claim 8 wherein the cells are selected from the group consisting of fibroblasts, tissue specific cells, progenitor cells, and stem cells.

12. (Currently Amended) The cell-matrix structure of claim 8 wherein the cells ~~are genetically engineered to produce the~~ anti-angiogenic molecule is selected from the group consisting of TSP-1, TSP-2, endostatin, angiostatin, and thrombospondin.

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13. (Currently Amended) The cell-matrix structure of claim 8 wherein the anti-angiogenic molecule is ~~thrombomodulin~~ TSP-2.
14. (Original) The cell-matrix structure of claim 8 wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule.
15. (Currently Amended) The cell-matrix structure of claim 8 wherein the cells are selected based on natural production of the ~~wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule and the cells are implanted at a site where the wherein the anti-angiogenic molecule is endogenous to the cells on the matrix and the cells are engineered to increase expression of the anti-angiogenic molecule in an amount effective to inhibit proliferation or cause tissue regression.~~
16. (Currently Amended) A method for treating a disorder characterized by excessive proliferation of tissue in a patient in need thereof comprising implanting a cell-matrix structure ~~in an amount sufficient to stop or regress the excessive tissue proliferation~~, wherein said the cell-matrix structure comprises a matrix having attached thereto cells that stably expressing a gene encoding a thrombospondin-2 (TSP-2) in an amount sufficient to stop or regress the excessive tissue proliferation.
17. (Previously Added) The method of claim 16, wherein the disorder is selected from the group consisting of malignant and benign neoplasias, vascular, inflammatory conditions causing excessive proliferation of cells, keloid formation, intraperitoneal or intrathoracic adhesions, endometriosis, congenital or endocrine abnormalities, psoriasis, unwanted skin proliferation, rheumatoid arthritis, multiple sclerosis, unwanted angiogenesis of the eye, restenosis, and infections causing excessive proliferation of cells.

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18. (Previously Added) The method of claim 16, wherein the matrix is selected from the group consisting of fibrous scaffolds, polymeric hydrogels, and micromachine or micromolded substrates.

19. (Previously Added) The method of claim 16, wherein the cells are selected from the group consisting of fibroblasts, tissue specific cells, progenitor cells, and stem cells.

20. (Previously Added) The method of claim 16, wherein the cells are genetically engineered to produce TSP-2.

21. (Previously Added) The method of claim 16, wherein TSP-2 is endogenous to the cells on the matrix and the cells are engineered to increase expression of TSP-2.

22. (Previously Added) The method of claim 16 wherein the cells are of a different cell type than the tissue that has proliferated.

23. (Previously Added) The method of claim 16 wherein the cells are selected based on natural production of TSP-2.

24. (Previously Added) The method of claim 1 wherein the cells are of a different cell type than the tissue that has proliferated.

25. (Previously Added) The method of claim 1 wherein the cells are selected based on natural production of the anti-angiogenic molecule.

26. (Previously Added) The method of claim 1 wherein the anti-angiogenic molecule is thrombomodulin.

27. (Previously Added) The method of claim 1 wherein the anti-angiogenic molecule is angiostatin.

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28. The method of claim 1 wherein the anti-angiogenic molecule is endostatin.
29. The method of claim 1 wherein the anti-angiogenic molecule is TSP-1.

Yu, Misook

From: TKOWALSKI@FLHLAW.COM
Sent: Tuesday, July 01, 2003 11:45 AM
To: Yu, Misook
Cc: Alwamoto@FLHLAW.COM
Subject: USSN 09/822,161 - further revised draft claim

Dear Examiner Yu,

Further to my telephone message, I am sorry that the overseas call I unexpectedly received took so long, and Michelle and I look forward to speaking with you at your early convenience. Here is a further suggestion for claim 1.

(Amended) A method for treating a disorder characterized by excessive tissue proliferation in a subject in need thereof comprising implanting a cell-matrix structure into the subject, wherein the cell-matrix structure comprises a matrix having attached thereto cells that stably express an anti-angiogenic molecule, in an amount effective to inhibit or regress the excessive tissue proliferation

Best regards.

Tom

Thomas J. Kowalski, Esq.
Admitted in New York

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